Towards the Modulation of RNA-Binding Proteins: New Compounds Targeting Protein HuR †

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RNA-binding proteins (RBPs) have been widely recognized for their pivotal role in the regulation of post-transcriptional processes. Particularly, their complexes with RNA are involved in numerous dysfunctions (*i.e.*, cancer, inflammation, and neurodegeneration) and thus pose the interesting question of whether they could be used as therapeutic targets with clinical relevance [1].

The research efforts of our team in this field have been dedicated to the identification of compounds able to modulate protein–RNA interactions, with a special focus on the ELAV (embryonic lethal abnormal vision) protein family [2,3]. Our first medicinal chemistry synthetic campaign exploited a structure-based approach for the design of novel HuR ligands based on different scaffolds. The synthesis of representative compounds of each series was accomplished through multicomponent reactions or equally efficient processes. Afterwards, the structural elucidation of their interaction with HuR was carried out according to an STD (saturation transfer difference)-NMR and *in silico* combined strategy [4].

In this communication, we move a step forward in understanding the structural features essential for the interaction with HuR. The information thus obtained represents the basis to identify compounds able to interfere with HuR–RNA complexes, therefore modulating gene expression.

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